

CHAPTER II

TRANSMITTAL LETTER
TO THE UNITED STATES ELECTED OFFICE (EO/US)
(ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)PCT/US97/15844 2 OCTOBER 1997 9 OCTOBER 1996
INTERNATIONAL APPLICATION NO. INTERNATIONAL FILING DATE PRIORITY DATE CLAIMEDA PROCESS FOR THE RECOVERY OF LACTIC ACID BY CONTACTING AQUEOUS SOLUTIONS
CONTAINING THE SAME WITH A BASIC ORGANIC EXTRACTANT

TITLE OF INVENTION

EYAL, Aharon Meir; GRUBER, Patrick, R.; FISHER, Rod, R.; KOLSTAD, Jeffrey, J.
APPLICANT(S)Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231
ATTENTION: EO/US

NOTE: The completion of those filing requirements that can be made at a time later than 30 months from the priority date results from the Commissioner exercising his judgment under the authority granted under 35 USC 371(d). The filing receipt will show the actual date of receipt of the last item completing the entry into the national phase. See 37 C.F.R. §1.491 which states: "An international application enters the national state when the applicant has filed the documents and fees required by 35 USC 371(c) within the periods set forth in § 1.494 and § 1.495."

WARNING: Where the items are those which can be submitted to complete the entry of the international application into the national phase are subsequent to 30 months from the priority date the application is still considered to be in the international state and if mailing procedures are utilized to obtain a date the express mail procedure of 37 C.F.R. §1.10 must be used (since international application papers are not covered by an ordinary certificate of mailing - See 37 C.F.R. §1.8).

NOTE: Documents and fees must be clearly identified as a submission to enter the national state under 35 USC 371 otherwise the submission will be considered as being made under 35 USC 111. 37 C.F.R. § 1.494(f).

1. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. 371:

CERTIFICATION UNDER 37 C.F.R. 1.10*

(Express Mail label number is mandatory.)

(Express Mail certification is optional.)

I hereby certify that this correspondence and the documents referred to as attached therein are being deposited with the United States Postal Service on this date April 8, 1999, in an envelope as "Express Mail Post Office to Addressee," Mailing Label Number EE784103730US, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

GERALDINE MARTI

(type or print name of person mailing paper)

Geraldine Marti
Signature of person mailing paper

WARNING: Certificate of mailing (first class) or facsimile transmission procedures of 37 C.F.R. 1.8 cannot be used to obtain a date of mailing or transmission for this correspondence.

***WARNING:** Each paper or fee filed by "Express Mail" must have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. 1.10(b)
"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will not be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.

- a. ☒ This express request to immediately begin national examination procedures (35 U.S.C. 371(f)).
- b. ☒ The U.S. National Fee (35 U.S.C. 371(c)(1)) and other fees (37 C.F.R. § 1.492) as indicated below:

2. Fees

CLAIMS FEE	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
<input type="checkbox"/> *	TOTAL CLAIMS	18 - 20 =	0	x \$ 18.00 =	\$
	INDEPENDENT CLAIMS	2 - 3 =	0	x \$ 78.00 =	
	MULTIPLE DEPENDENT CLAIM(S) (if applicable) + \$260.00				
BASIC FEE**	<input type="checkbox"/> U.S. PTO WAS INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where an International preliminary examination fee as set forth in § 1.482 has been paid on the international application to the U.S. PTO: <input type="checkbox"/> and the international preliminary examination report states that the criteria of novelty, inventive step (non-obviousness) and industrial activity, as defined in PCT Article 33(2) to (4) have been satisfied for all the claims presented in the application entering the national stage (37 CFR 1.492(a)(4)) \$96.00 <input type="checkbox"/> and the above requirements are not met (37 CFR 1.492(a)(1)) \$670.00 <input type="checkbox"/> U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in § 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in § 1.445(a)(2) to the U.S. PTO: <input type="checkbox"/> has been paid (37 CFR 1.492(a)(2)) \$760.00 <input type="checkbox"/> has not been paid (37 CFR 1.492(a)(3)) \$970.00 <input checked="" type="checkbox"/> where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 CFR 1.492(a)(5)) \$840.00				
	Total of above Calculations				= \$840.00
SMALL ENTITY	Reduction by 1/3 for filing by small entity, if applicable. Affidavit must be filed. (note 37 CFR 1.9, 1.27, 1.28)				
	Subtotal				\$840.00
	Total National Fee				\$840.00
	Fee for recording the enclosed assignment document \$40.00 (37 CFR 1.21(h)). (See Item 13 below). See attached "ASSIGNMENT COVER SHEET".				
TOTAL	Total Fees enclosed				\$840.00

*See attached Preliminary Amendment Reducing the Number of Claims.

- i. ☒ A check in the amount of \$840.00 to cover the above fees is enclosed.
- ii. ☐ Please charge Account No. _____ in the amount of \$ _____.
 A duplicate copy of this sheet is enclosed.

****WARNING:** "To avoid abandonment of the application the applicant shall furnish to the United States Patent and Trademark Office not later than the expiration of 30 months from the priority date: * * * (2) the basic national fee (see § 1.492(a)). The 30-month time limit may not be extended." 37 C.F.R. § 1.495(b).

WARNING: If the translation of the international application and/or the oath or declaration have not been submitted by the applicant within thirty (30) months from the priority date, such requirements may be

met within a time period set by the Office. 37 C.F.R. § 1.495(b)(2). The payment of the surcharge set forth in § 1.492(e) is required as a condition for accepting the oath or declaration later than thirty (30) months after the priority date. The payment of the processing fee set forth in § 1.492(f) is required for acceptance of an English translation later than thirty (30) months after the priority date. Failure to comply with these requirements will result in abandonment of the application. The provisions of § 1.136 apply to the period which is set. Notice of Jan. 3, 1993, 1147 O.G. 29 to 40.

3. ☒ A copy of the International application as filed (35 U.S.C. 371(c)(2)):

NOTE: Section 1.495 (b) was amended to require that the basic national fee and a copy of the international application must be filed with the Office by 30 months from the priority date to avoid abandonment "The International Bureau normally provides the copy of the international application to the Office in accordance with PCT Article 20. At the same time, the International Bureau notifies applicant of the communication to the Office. In accordance with PCT Rule 47.1, that notice shall be accepted by all designated offices as conclusive evidence that the communication has duly taken place. Thus, if the applicant desires to enter the national stage, the applicant normally need only check to be sure the notice from the International Bureau has been received and then pay the basic national fee by 30 months from the priority date." Notice of Jan. 7, 1993, 1147 O.G. 29 to 40, at 35-36. See item 14c below.

- a. ☒ is transmitted herewith.
b. ☒ is not required, as the application was filed with the United States Receiving Office.
c. ☐ has been transmitted
i. ☐ by the International Bureau.
Date of mailing of the application (from form PCT/IB/308): _____.
ii. ☐ by applicant on _____.
Date

4. ☒ A translation of the International application into the English language (35 U.S.C. 371(c)(2)):

- a. ☐ is transmitted herewith.
b. ☒ is not required as the application was filed in English.
c. ☐ was previously transmitted by applicant on _____.
Date
d. ☐ will follow.

5. ☒ Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. 371(c)(3)):

NOTE: The Notice of January 7, 1993 points out that 37 C.F.R. § 1.495(a) was amended to clarify the existing and continuing practice that PCT Article 19 amendments must be submitted by 30 months from the priority date and this deadline may not be extended. The Notice further advises that: "The failure to do so will not result in loss of the subject matter of the PCT Article 19 amendments. Applicant may submit that subject matter in a preliminary amendment filed under section 1.121. In many cases, filing an amendment under section 1.121 is preferable since grammatical or idiomatic errors may be corrected." 1147 O.G. 29-40, at 36.

- a. ☐ are transmitted herewith.
b. ☐ have been transmitted
i. ☐ by the International Bureau.
Date of mailing of the amendment (from form PCT/IB/308): _____.
ii. ☐ by applicant on _____.
Date
c. ☒ have not been transmitted as
i. ☒ applicant chose not to make amendments under PCT Article 19.
Date of mailing of Search Report (from form PCT/ISA/210): April 4, 1998
ii. ☐ the time limit for the submission of amendments has not yet expired.
The amendments or a statement that amendments have not been made will be transmitted before the expiration of the time limit under PCT Rule 46.1.

6. [X] A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. 371(c)(3)):
- [] is transmitted herewith.
 - [] is not required as the amendments were made in the English language.
 - [X] has not been transmitted for reasons indicated at point 5(c) above.
7. [X] A copy of the international examination report (PCT/IPEA/409)
- [X] is transmitted herewith.
 - [X] is not required as the application was filed with the United States Receiving Office.
8. [X] Annex(es) to the international preliminary examination report
- [X] is/are transmitted herewith.
 - [X] is/are not required as the application was filed with the United States Receiving Office.
9. [X] A translation of the annexes to the international preliminary examination report
- [] is transmitted herewith.
 - [X] is not required as the annexes are in the English language.
10. [X] An oath or declaration of the inventor (35 U.S.C. 371(c)(4)) complying with 35 U.S.C. 115
- [] was previously submitted by applicant on _____.
Date
 - [X] is submitted herewith, and such oath or declaration
 - [] is attached to the application.
 - [] identifies the application and any amendments under PCT Article 19 that were transmitted as stated in points 3(b) or 3(c) and 5(b); and states that they were reviewed by the inventor as required by 37 C.F.R. 1.70.
 - [X] will follow.

Other document(s) or information included:

11. [X] An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a):
- [X] is transmitted herewith.
 - [] has been transmitted by the International Bureau.
Date of mailing (from form PCT/IB/308): _____.
 - [] is not required, as the application was searched by the United States International Searching Authority.
 - [] will be transmitted promptly upon request.
 - [] has been submitted by applicant on _____.
Date
12. [X] An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98:
- [X] is transmitted herewith.
Also transmitted herewith is/are:
[X] Form PTO-1449 (PTO/SB/08A and 08B).
[X] Copies of citations listed.
 - [] will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. 371(c).
 - [] was previously submitted by applicant on _____.
Date

13. ☐ An assignment document is transmitted herewith for recording.

A separate ☐ "COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION" or ☐ FORM PTO 1595 is also attached.

14. ☒ Additional documents:
- a. ☒ Copy of request (PCT/RO/101)
 - b. ☒ International Publication No. WO 98/15517
 - i. ☒ Specification, claims and drawing
 - ii. ☐ Front page only
 - c. ☐ Preliminary amendment (37 C.F.R. § 1.121)
 - d. ☒ Other

(IPEA/402) Notification of Receipt of Demand

(IPEA/408) Written Opinion

Reply to Written Opinion of November 3, 1998

15. ☒ The above checked items are being transmitted
- a. ☒ before 30 months from any claimed priority date.
 - b. ☐ after 30 months.
16. ☐ Certain requirements under 35 U.S.C. 371 were previously submitted by the applicant on _____, namely:

AUTHORIZATION TO CHARGE ADDITIONAL FEES

WARNING: *Accurately count claims, especially multiple dependent claims, to avoid unexpected high charges if extra claims are authorized.*

NOTE: *"A written request may be submitted in an application that is an authorization to treat any concurrent or future reply, requiring a petition for an extension of time under this paragraph for its timely submission, as incorporating a petition for extension of time for the appropriate length of time. An authorization to charge all required fees, fees under § 1.17, or all required extension of time fees will be treated as a constructive petition for an extension of time in any concurrent or future reply requiring a petition for an extension of time under this paragraph for its timely submission. Submission of the fee set forth in § 1.17(a) will also be treated as a constructive petition for an extension of time in any concurrent reply requiring a petition for an extension of time under this paragraph for its timely submission." 37 C.F.R. § 1.136(a)(3).*

NOTE: *"Amounts of twenty-five dollars or less will not be returned unless specifically requested within a reasonable time, nor will the payer be notified of such amounts; amounts over twenty-five dollars may be returned by check or, if requested, by credit to a deposit account." 37 C.F.R. § 1.26(a).*

- ☒ The Commissioner is hereby authorized to charge the following additional fees that may be required by this paper and during the entire pendency of this application to Account No. 12-0425.

☒ 37 C.F.R. 1.492(a)(1), (2), (3), and (4) (filing fees)

WARNING: Because failure to pay the national fee within 30 months without extension (37 C.F.R. § 1.495(b)(2)) results in abandonment of the application, it would be best to always check the above box.

☐ 37 C.F.R. 1.492(b), (c) and (d) (presentation of extra claims)

NOTE: Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 C.F.R. § 1.492(d)), it might be best not to authorize the PTO to charge additional claim fees, except possible when dealing with amendments after final action.

☒ 37 C.F.R. 1.17 (application processing fees)

☐ 37 C.F.R. 1.17(a)(1)-(5)(extension fees pursuant to § 1.136(a).

☒ 37 C.F.R. 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. 1.311(b))

NOTE: Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 C.F.R. § 1.311(b).

NOTE: 37 C.F.R. 1.28(b) requires "Notification of any change in loss of entitlement to small entity status must be filed in the application . . . prior to paying, or at the time of paying . . . issue fee." From the wording of 37 C.F.R. § 1.28(b): (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.

☒ 37 C.F.R. § 1.492(e) and (f) (surcharge fees for filing the declaration and/or filing an English translation of an International Application later than 30 months after the priority date).



SIGNATURE OF PRACTITIONER

Reg. No.:25,858

William R. Evans

(type or print name of practitioner)

Tel. No.: (212) 708-1930

c/o Ladas & Parry

26 West 61st Street

P.O. Address

Customer No.:

New York, NY 10023

PROCESS FOR THE RECOVERY OF LACTIC ACID

The present invention relates to a process for the recovery of lactic acid. More particularly, the present invention relates to a process for the recovery of lactic acid and products thereof from an aqueous solution containing free lactic acid and at least one lactate salt.

Lactic acid has long been used as a food additive and in various chemical and pharmaceutical applications. More recently, lactic acid has been used in the making of biodegradable polylactic acid polymers as a replacement for present plastic materials, as well as for various new uses where biodegradability is needed or desired. Accordingly, there is an ever-increasing demand for lactic acid. The present invention aims at meeting this demand by providing an efficient and environmentally friendly process for producing lactic acid which avoids the consumption of bases and acids and substantially reduces, if not eliminates, the formation of waste or byproduct salts.

The production of lactic acid is commonly carried out by fermentation of a strain of the bacterial genus *Lactobacillus*, and, for example, more particularly by the species *Lactobacillus delbrueckii* or *Lactobacillus acidophilus*. In general, the production of lactic acid by fermentation in a fermentation broth is well-known in the art. The fermentation substrate consists of carbohydrates together with suitable mineral and proteinaceous nutrients. Because the lactic acid-producing microorganisms are inhibited in a strongly acidic environment, lactic acid fermentation is usually conducted at about neutral pH and a neutralizing agent is added for pH adjustment. As the pKa of lactic acid is 3.86, at the pH of fermentation, practically only lactate salts exist. Thus, recovery of lactic acid in an acid form from the fermentation

liquor requires chemical conversion. Several processes were developed for such conversion.

In some of the processes, the conversion liberates lactic acid in solution, e.g., by displacement with a strong acid. Thus, when calcium bases are used as the neutralizing agents in the fermentation, calcium lactate is formed. Reacting the calcium lactate-containing fermentation liquor with sulfuric acid results in precipitation of gypsum and liberation of lactic acid in the solution.

Nakanishi and Tsuda, in JP 46/30176, consider production of 1-butyl lactate by extraction of an acidified crude fermentation broth with 1-butanol, followed by esterification of the extract phase. BASF (EP-0 159 585) considers a similar process with isobutanol, to form isobutyl lactate. The process of WO 93/00440, assigned to DuPont, comprises the steps of: (1) simultaneously mixing a strong acid, an alcohol, and a concentrated fermentation broth which contains mainly basic salts of lactic acid, which react to form a crystal precipitate comprising basic salts of the strong acid and an impure lactate ester of the alcohol; (2) removing water from the mixture as a water/alcohol azeotrop, which can be accomplished either sequentially or substantially simultaneously with step (1); (3) removing the crystal precipitate from the mixture; and (4) distilling the impure lactate ester to remove impurities and recovering the high purity ester.

Alternatively to purifying the lactic acid, which is liberated by displacement with a strong acid through esterification and distillation of the ester, one could purify it by extraction. The extractant could be a relatively weak one, and would allow the recovery of the extracted HLA at a high concentration by back-extraction. The known, and food-approved, weak

extractants to be considered are amine-based or solvating extractants. One may consider esters, ethers, ketones, aldehydes, etc., but alkanols seem to be preferable.

Out of these two groups of weak extractants, the amine-based ones are more attractive, but they would not work in a simple process wherein the stronger than lactic displacing acid is added to the lactate salt-containing solution and the liberated HLa is directly extracted by contact with the extractant. The amine-based extractant prefers the stronger acid in a mixture, and would therefore reverse the reaction, removing the added acid.

Liquid-liquid extraction (LLE) proved to be an efficient way for recovering acidic fermentation products from fermentation liquors. Thus, a large fraction of the world's citric acid production uses an LLE process which recovers the acid from the broth by extraction with an extractant composed of a water-immiscible amine in a diluent. This extractant combines high recovery yields and high selectivity, resulting in a pure product and reversibility.

Baniel and co-inventors (U.S. Patent Application 4,275,234) have found that the extracted acid can be recovered from the acid-containing extract by back-extraction with water. They have also found that, if the back-extraction is conducted at a temperature higher than that of the extraction, the concentration of the acid in the back-extract (the aqueous product of the back-extraction) could be significantly higher than that in the broth. Thus, in addition to the recovery at high yield and purity, extraction by an amine-based extractant provides for concentration of the recovered product and thereby for saving in energy consumption. An amine-based extractant similar to the one used in the citric acid process would be suitable for extraction of free lactic acid.

In some recently published patents, LLE is applied for salt-splitting. Thus, in U.S. Patent 5,132,456 (King), a strongly basic extractant extracts part of the lactic acid from the neutral solution, which results in a lactic acid-loaded extractant and a basic solution. This basic solution, which still contains most of the lactic acid values, could be recycled as a neutralizing medium to the fermentation. In U.S. Patent No. 5,510,526 (Baniel), the extraction of the acid is conducted under CO₂ pressure so that a bicarbonate is formed. The latter can be used as a neutralizing agent in the fermentation. In order to limit the CO₂ pressure to an economic one and still achieve high yields, the extractant used should be quite strong.

Recently, new strains have been developed for lactic acid fermentation which can operate at slightly acidic conditions. It is expected that the fermentation pH will be further lowered on future development, probably at the cost of lowering the overall concentration in the solution. As long as the pH of the broth is >5 , practically all of the product is still in the salt form. However, at a lower pH, a fraction of the lactic acid in the broth is not neutralized. Thus, at pH of 4.8 and 3.8, about 10% and about 50%, respectively, could be considered as being in free acid form.

It would not be expected that free lactic acid could be extracted efficiently from the lactate salt-containing broth by an amine-based extractant, due to the buffering effect of the salt. Amines extract acids through ion-pair formation and should therefore be positively charged. In the case of primary, secondary and tertiary amines (quaternary ones are not suitable for reversible extraction), the formation of the required positive charge is by binding protons (protonation) from the aqueous solution. Extraction efficiency is therefore determined by the availability of protons in the aqueous solution. Thus, extraction of the free lactic acid is strongly dependent on the concentration of the lactate salts in the solution:

$$[H] = K_a[HLa]/[La]$$

where $[H]$, $[HLa]$ and $[La]$ denote the concentration of protons, undissociated lactic acid and lactate ions, respectively, and K_a is the dissociation constant of lactic acid. A significant lactate salt to free lactic acid ratio, or low free acid to salt ratio, substantially decreases the ratio $[HLa]/[La]$ and thereby decreases the availability of protons in the aqueous solution and the protonation of the amine. Therefore, the efficiency of extraction of the free lactic acid is expected to be low. It would be even lower, if the extractant already contains lactic acid from a previous stage.

Recovery of the free lactic acid from the fermentation liquor by LLE, if feasible, would still leave lactate values, i.e., lactic acid and lactate salts, in the aqueous solution. Recycling of those values back to the fermentation is feasible, but quite problematic and costly, for several reasons: (a) since a complete recycle would build up impurities in the system, a bleed would be required, and treatment of the bleed stream would be needed to avoid significant losses; (b) a separate operation may be needed for the removal of traces of extractant from the recycled stream; (c) there would probably be a

need to sterilize the recycle stream; and (d) water distillation from the recycled stream may be needed to maintain the water balance.

Alternatively, one can operate one of the salt-splitting processes for the recovery of lactic acid from the salts. If LLE processes are chosen, an extract loaded with lactic acid would be formed. Back-extraction of the lactic acid from this extract, as well as from the extract formed on the extraction of the free lactic acid, would be required. The lactic acid concentration in both extracts is expected to be low, due to the low activity of the lactic acid in the source from which it is extracted. That is particularly true for the salt-splitting process. The concentration of the lactic acid in the back-extract is therefore expected to be low.

U.S. Patent 5,132,456 suggests a way to recover extracted carboxylic acid from extracts formed on LLE-based salt-splitting. It comprises leaching or back-extraction with an aqueous solution of ammonia or low molecular weight alkyl amine, especially trimethyl amine (TMA). The resultant aqueous ammonium or alkylammonium carboxylate solution can be concentrated, if necessary, and the carboxylate can be decomposed thermally to yield the product carboxylic acid and ammonia or amine, which can be condensed and recycled. This process is costly and complex, and is particularly problematic for recovery of extracted lactic acid, as stated in said patent:

"For lactic acid, the decomposition is incomplete, being stopped by the formation of a viscous, almost glassy mass containing polymerized lactic acid along with substantial TMA and water. There are, however, effective ways of driving the decomposition to completion for lactic acid, such as diluting the viscous mass with an appropriate solvent (e.g., methyl isobutyl ketone) and continuing the heating and decomposition process."

With the above state of the art in mind, it has now been surprisingly found that a basic extractant is capable of extracting most of the free acid from a fermentation liquor, even if the free lactic acid to lactate salt ratio in it is lower than 1:3. Furthermore, high yield of extraction was found, even with an extractant that comprises lactic acid from a previous step.

Thus, according to the present invention, there is provided a process for the recovery of lactic acid and products thereof from an aqueous solution containing free lactic acid and at least one lactate salt at a total concentration of at least 5%, said process comprising the steps of: (a) extracting at least 70% of the free lactic acid from said aqueous solution by contacting said solution with a basic extractant, to form a lactic acid-containing extract and a lactic acid-depleted, lactate salt-containing aqueous solution; (b) separating said lactic acid-containing extract from said depleted aqueous solution; and (c) stripping the extracted lactic acid from said extract by methods known per se, to form a solution of lactic acid and a stripped extractant.

In a preferred embodiment of the present invention said process further comprises the step of (d) recovering lactic acid and products thereof from said lactate salt in said lactic acid-depleted aqueous solution by methods known per se.

Preferably said process is carried out on an aqueous solution containing free lactic acid and at least one lactate salt wherein the ratio between said free lactic acid and said lactate salt is between 1:9 and 5:1, and most preferably on an aqueous solution wherein the ratio between said free lactic acid and said lactate salt is between 1:9 and 3:1.

In an especially preferred embodiment of the present invention said basic extractant comprises a portion of lactic acid, preferably at least 3% lactic acid extracted in a previous step, and said solution is contacted with said extractant to form an extract comprising lactic acid in an amount greater than said portion and a lactic acid-depleted, lactate salt-containing aqueous solution. In especially preferred embodiments of the present invention the basic extractant used in step (a) comprises at least 5% lactic acid extracted in previous step.

Preferably said basic extractant in step (a) has a basicity corresponding to a pKa lower than 7 and in especially preferred embodiments of the present invention said basic extractant has a basicity corresponding to a pKa lower than 6.

In a further preferred embodiment of the invention, both the extraction of the free acid from the broth and the salt-splitting of the lactate salt left in the solution are conducted by LLE with a basic extractant. It is further preferred to use an extractant comprising amine for both, and even more preferred to use extractants comprising the same amine, so that the same extractant could be used, as is or after some adjustment, in both extractions.

In yet a further preferred embodiment of the invention, the process comprises the steps of: (a) extracting most of the free lactic acid from a fermentation liquor comprising the free acid and a lactate salt by an extractant recycled from a previous step; (b) stripping the lactic acid loaded extractant obtained, preferably by back-extraction with water, at a temperature higher than that of the extraction, to form purified lactic acid solution and a stripped extractant; and (c) using the stripped extractant to recover lactic acid from the lactate salt-containing, lactic acid-depleted aqueous solution formed in step

(a). The lactic acid-containing extractant formed in step (c) is suitable for extraction of free lactic acid from additional fermentation liquor, according to step (a).

The advantages of the process of the preferred embodiment of the invention include the following: (1) recovery of lactate values from the free acid fraction and salt-splitting are effected by LLE, which ensures high recovery yields, high purity, and relatively high product concentrations; (2) there is no need to operate two separate extraction cycles; (3) the stripped extractant, which has the strongest extraction power, is utilized where the strong extraction power is mostly needed, i.e., for the salt-splitting; (4) the surprising finding that even a partially loaded extractant is capable of efficient extraction of the free lactic acid in the presence of lactate salt is best utilized; and (5) an extract containing lactic acid from both the free lactic acid and the salt-splitting is fed to the stripping operation in an overall high concentration, so that the concentration of the back-extract is high. Such high concentrations of back-extract are not attainable by operating the salt-splitting separately and stripping at the same conditions. Neither can they be obtained by operating the salt-splitting and the recovery of the free acid in two separate cycles and mixing the extract for back-extraction, nor by back-extracting them separately and mixing the back-extracts.

The preferred amines for the extractant are chosen from the group consisting of primary, secondary and tertiary amines, with a total number of at least 18 carbon atoms. Mostly preferred are tertiary amines. A diluent is usually used to achieve the required physical properties.

The basicity of the extractant is easily adjusted by adding a polar solvent to the extractant. Such polar solvents enhance the extraction efficiency

of the amine, which is the main active component, and are usually referred to as "enhancers." Alkanols provide very efficient enhancers. The basicity of the extractant is thus adjusted by the amount of enhancer therein, or, more precisely, by the enhancer to amine molar ratio.

The basicity of water-soluble bases is easily determined by their degree of dissociation in aqueous solution. The basicity of water-immiscible extractants is determined indirectly, through their interaction with solutes in an aqueous solution. Thus, the apparent basicity of highly basic extractants can be compared by contacting them with aqueous solutions of NaCl and determining the pH of the aqueous solution in equilibrium. The higher the pH is, the stronger is the apparent basicity of the extractant. For comparing extractants of medium or weak basicity, equilibration with acid solutions is preferred. Unlike water-soluble bases, the apparent basicity found for water-immiscible extractants is determined, in addition to the properties of the amine, by the acid in the aqueous solution, by steric hindrance to extraction, and by the diluents of the amine.

While improving the extraction, the presence of an enhancer interferes in the back-extraction. The proportion of the enhancer in the solution should therefore be adjusted, to provide for high yields in the extraction and efficient back-extraction, resulting in lactic acid solutions of high concentration. It is also possible to remove at least a part of the enhancer prior to back-extraction.

As explained hereinabove, the basicity of the extractant used in the salt-splitting should be quite high. Extraction of the free acid, on the other hand, can be conducted with a weaker extractant. A process combining salt-splitting

with the recovery of the free acid could be operated in several ways, including the following:

1. Two separate extraction and back-extraction cycles can be operated.
2. Two extractions can be operated; the extracts are combined; at least part of the enhancer is removed; the resulting organic phase is back-extracted; the stripped organic phase is split into two streams; the enhancer content of each stream is adjusted to the required level, and each stream is used again in the separate extraction.
3. The extraction may be operated according to the above-described preferred process, where the stripped extractant is used first in the salt-splitting conducted on the lactic acid-depleted solution, and then for the extraction of the free lactic acid of a fresh solution.

It would have been expected that adjustment of the extractant composition would be needed in process 3 above, e.g., by adding enhancer to the extractant after stripping and prior to the salt-splitting operation, and removing some enhancer prior to the extraction of the free lactic acid. It was surprisingly found that such an adjustment is not necessary.

In preferred embodiments of the present invention, the stripped extractant formed in step (c) of the process is used as is, or after some adjustment, as the extractant in step (d), and the lactic acid-containing extractant formed in step (d) is used as is, or after some adjustment, as the extractant in step (a), wherein said adjustment comprises adding or removing a polar solvent.

While the invention will now be described in connection with certain preferred embodiments in the following examples so that aspects thereof may be more fully understood and appreciated, it is not intended to limit the

invention to these particular embodiments. On the contrary, it is intended to cover all alternatives, modifications and equivalents as may be included within the scope of the invention as defined by the appended claims. Thus, the following examples which include preferred embodiments will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of example and for purposes of illustrative discussion of preferred embodiments of the present invention only and are presented in the cause of providing what is believed to be the most useful and readily understood description of formulation procedures as well as of the principles and conceptual aspects of the invention.

EXAMPLES

Example 1

An extractant containing 48 wt% tricaprylyl amine (Henkel's Alamine 336), 30 wt% octanol and 22 wt% kerosene was prepared by mixing the components at the desired ratio. A starting aqueous solution was prepared by mixing solutions of sodium lactate and lactic acid so that their final concentrations were 2.9 and 1.5 mol/Kg respectively (lactic acid to sodium lactate molar ratio of 1:1.9).

The aqueous solution was equilibrated at ambient temperature with three successive portions of the organic phase. Each equilibration was at aqueous to organic wt ratio of 2:1. The phases were then separated and analyzed for their lactic acid content.

The results show that 83% of the lactic acid in the aqueous phase was extracted.

Example 2

An extractant containing 48 wt% tricaprylyl amine (Henkel's Alamine 336), 20 wt% octanol and 32 wt% kerosene was prepared by mixing the components at the desired ratio. A starting aqueous solution was prepared by mixing solutions of sodium lactate and lactic acid so that their final concentrations were 1.7 and 2.8 mol/Kg respectively (lactic acid to sodium lactate molar ratio of 1:0.61).

The aqueous solution was equilibrated at ambient temperature with a portion of the organic phase. The phases were then separated and analyzed for their lactic acid content. The resulting aqueous phase was equilibrated with another portion of the organic phase, separated and analyzed. These operations were repeated several times.

The equilibrium lactic acid concentrations (mol/Kg) in the successive contacts in the aqueous and organic phases, respectively, were:

- 1) 2.3 and 1.9;
- 2) 1.6 and 1.7;
- 3) 0.93 and 1.43;
- 4) 0.23 and 0.83; and
- 5) 0.05 and 0.28.

Example 3

The procedure of Example 2 was repeated, except that the starting composition of the aqueous phase was 1.6 mol/Kg lactic acid and 1.0 mol/Kg sodium lactate. The equilibrium lactic acid concentrations (mol/Kg) in the successive contacts in the aqueous and organic phases, respectively, were:

- 1) 1.1 and 1.56;
- 2) 0.61 and 1.3;
- 3) 0.29 and 0.98;

- 4) 0.11 and 0.53; and
- 5) 0.03 and 0.187.

Example 4

The procedure in Example 2 was repeated, except that the starting composition of the aqueous phase was 0.9 mol/Kg lactic acid and 0.4 mol/Kg sodium lactate. The equilibrium lactic acid concentrations (mol/Kg) in the successive contacts in the aqueous and organic phases, respectively, were:

- 1) 0.24 and 0.79;
- 2) 0.096 and 0.395; and
- 3) 0.028 and 0.185.

Example 5

The procedure in Example 2 was repeated, except that the starting composition of the aqueous phase was 0.71 mol/Kg lactic acid and 0.32 equ/Kg calcium lactate. The equilibrium lactic acid concentrations (mol/Kg) in the successive contacts in the aqueous and organic phases, respectively, were:

- 1) 0.37 and 1.16;
- 2) 0.14 and 0.33; and
- 3) 0.009 and 0.1.

The results in Examples 1 to 5 show that nearly all the free lactic acid can be extracted from solutions comprising it along with lactate salts. This is true for various starting concentrations and acid to salt molar ratios. The distribution coefficients were high.

Example 6

An aqueous solution containing 1.2 mol/Kg lactic acid and 1.5 mol/Kg sodium lactate was counter-currently extracted with an extractant composed of 48 wt% tricaprylyl amine (Henkel's Alamine 336), 30 wt% octanol and 22 wt% kerosene. The organic to aqueous phase ratio was 1:1 wt/wt. In four stages, the extraction of the free acid was nearly completed. The lactic acid concentration in the extract formed was 1.1 mol/Kg. The extract was counter-currently back-extracted with water at 140°C. The organic to aqueous ratio was 1:0.8 wt/wt. In six stages, most of the acid was back-extracted from the extractant to form an aqueous solution of 1.25 mol/Kg lactic acid.

Example 7

The experiment in Example 6 was repeated, except that the composition of the aqueous phase was 0.7 mol/Kg lactic acid and 0.32 equ/Kg calcium lactate. The organic to aqueous ratio in the extraction was 0.87:1. The loaded extractant contained 0.7 mol/Kg lactic acid. Back-extraction in conditions similar to those in Example 6 resulted in a 0.7 mol/Kg lactic acid solution.

Concentrated sulfuric acid solution was added dropwise to the aqueous solution resulting from the extraction step, in an amount equivalent to the calcium ion content. The precipitated gypsum was removed by decantation. The resulting aqueous solution was extracted with an extractant composed as above. Practically all the lactate values in the aqueous solution were extracted as lactic acid, which was then recovered from the organic phase by back-extraction.

Example 8

An aqueous starting solution containing 2.5 mol/Kg lactic acid and 2.5 mol/Kg sodium lactate was extracted with an extractant composed as in Example 1. Practically all the lactic acid was extracted. The remaining aqueous phase was concentrated to 5 mol/Kg sodium lactate and extracted by a fresh extractant of similar composition. In organic to aqueous wt/wt ratio of 7:1, under CO₂ pressure of 30 atmospheres, most of the lactate values were extracted as lactic acid in eight stages. The extract obtained, comprising about 0.7 mol/Kg lactic acid, was used to extract lactic acid from another portion of the starting aqueous solution containing lactic acid. At organic to aqueous ratio of 2:1 wt/wt and six stages, more than 80% of the acid was extracted. The lactic acid concentration in the obtained extract was 1.7 mol/Kg. Back-extraction at 150°C resulted in a 14% lactic acid solution.

It will be evident to those skilled in the art that the invention is not limited to the details of the foregoing illustrative examples and that the present invention may be embodied in other specific forms without departing from the essential attributes thereof, and it is therefore desired that the present embodiments and examples be considered in all respects as illustrative and not restrictive, reference being made to the appended claims, rather than to the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

2024102509

Article 31
Amendment

00001001000000

1. A process for the recovery of lactic acid and products thereof from an aqueous solution containing free lactic acid and at least one lactate salt at a total concentration of at least 5%, said process comprising the steps of:
 - (a) extracting at least 70% of the free acid from said aqueous solution by contacting said acid-depleted, lactate salt-containing aqueous solution;
 - (b) separating said lactic acid-containing extract from said depleted aqueous solution;
 - (c) stripping said extracted lactic acid from said extract by methods known per se, to form a solution of lactic acid and stripped basic extractant;
 - (d) recovering lactic acid and products thereof from said lactate salt in said lactic acid-depleted aqueous solution by a method comprising extraction with a basic extractant, substantially as obtained in step (c), to form lactic acid containing extractant; and
 - (e) using said lactic acid-containing extractant from step (d), substantially as is, as said basic extractant in step (a).
2. A process according to claim 1, wherein the ratio between said free lactic acid and said lactate salt is between 1:9 and 5:1.
3. A process according to claim 1, wherein the ratio between said free lactic acid and said lactate salt is between 1:9 and 3:1.
4. A process according to claim 1, wherein said basic extractant comprises a portion of lactic acid and said solution is contacted with said extractant to form an extract comprising lactic acid in an amount greater than said portion and a lactic acid-depleted, lactate salt-containing aqueous solution.
5. A process according to claim 1, wherein said adjustment comprises adding a polar solvent.
6. A process according to claim 1, wherein said adjustment comprises removing a polar solvent.
7. A process according to claim 1, wherein the ratio of free lactic acid to lactate salt is up to 2:1.
8. A process according to claim 1, wherein the basic extractant used in step (a) comprises at least 3% of the lactic acid extracted in a previous step.
9. A process according to claim 1, wherein said aqueous solution is concentrated by water evaporation prior to step (a).

10. A process according to claim 1, wherein said aqueous solution containing free lactic acid and lactate salt is a result of fermentation.
11. A process according to claim 1, wherein said lactate salt is selected from the group consisting of calcium lactate, sodium lactate and ammonium lactate.
12. A process according to claim 1, wherein said basic extractant in step (a) has a basicity corresponding to pKa lower than 7.
13. A process according to claim 1, wherein:
- said basic extractant in step (a) is recycled from a previous step;
 - said lactic acid-loaded extract obtained in step (a) is stripped to form a solution of purified lactic acid and said stripped extractant;
 - said stripped extractant obtained in step (c) is used for the recovery of lactic acid from said lactate salt in step (d); and
 - the lactic acid-comprising extract formed in step (d) is used for extraction of free lactic acid in step (a).
14. A process according to claim 1, wherein said recovery of lactic acid from said lactate salt in step (a) is effected under CO₂ pressure.
15. A process according to claim 1, wherein said recovery of lactic acid and products thereof from said lactate salt in said lactic acid-depleted aqueous solution is achieved by using an acid stronger than lactic acid.
16. A process according to claim 14, wherein said stronger acid is sulfuric acid, and a sulfate salt is formed as a by-product.
17. A process according to claim 1, wherein said recovery of lactic acid and products thereof from said lactate salt in said lactic acid-depleted aqueous solution is achieved through the use of electric energy.
18. A process for the recovery of lactic acid and products thereof from an aqueous solution containing free lactic acid and at least one lactate salt at a total concentration of at least 5%, said process comprising the steps of:
- (a) extracting at least 70% of the free acid from said aqueous solution by contacting said acid-depleted, lactate salt-containing aqueous solution;
 - (b) separating said lactic acid-containing extract from said depleted aqueous solution;
 - (c) stripping said extracted lactic acid from said extract by methods known per se, to form a solution of lactic acid and stripped basic extractant;

(d) recovering lactic acid and products thereof from said lactate salt in a portion of said lactic acid-depleted aqueous solution by a method comprising extraction with a basic extractant, substantially as obtained in step (c), to form lactic acid containing extractant; and

(e) using said lactic acid-containing extractant from step (d), substantially as is, as said basic extractant in step (a).

0326160, 102592

A PROCESS FOR THE RECOVERY OF LACTIC ACID

ABSTRACT OF THE DISCLOSURE

The invention provides a process for the recovery of lactic acid and products thereof from an aqueous solution containing free lactic acid and at least one lactate salt at a total concentration of at least 5%, the process comprising the steps of: extracting at least 70% of the free lactic acid from the aqueous solution by contacting the solution with a basic extractant, to form a lactic acid-containing extract and a lactic acid-depleted, lactate salt-containing aqueous solution; separating the lactic acid-containing extract from the depleted aqueous solution; and stripping the extracted lactic acid from the extract by methods known per se, to form a solution of lactic acid and a stripped extractant.

Practitioner's Docket No. U 012190-3

PATENT

COMBINED DECLARATION AND POWER OF ATTORNEY

(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL,
CONTINUATION, OR C-I-P)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is of the following type:

(check one applicable item below)

- ☐ original.
☐ design.
☐ supplemental.

NOTE: If the declaration is for an international Application being filed as a divisional, continuation or continuation-in-part application, do not check next item; check appropriate one of last three items.

- ☒ national stage of PCT.

NOTE: If one of the following 3 items apply, then complete and also attach **ADDED PAGES FOR DIVISIONAL, CONTINUATION OR C-I-P**.

NOTE: See 37 C.F.R. § 1.63(d) (continued prosecution application) for use of a prior nonprovisional application declaration in the continuation or divisional application being filed on behalf of the same or fewer of the inventors named in the prior application.

- ☐ divisional.
☐ continuation.

NOTE: Where an application discloses and claims subject matter not disclosed in the prior application, or a continuation or divisional application names an inventor not named in the prior application, a continuation-in-part application must be filed under 37 C.F.R. § 1.53(b) (application filing requirements-nonprovisional application).

- ☐ continuation-in-part (C-I-P).

INVENTORSHIP IDENTIFICATION

WARNING: If the inventors are each not the inventors of all the claims, an explanation of the facts, including the ownership of all the claims at the time the last claimed invention was made, should be submitted.

My residence, post office address and citizenship are as stated below, next to my name. I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter that is claimed, and for which a patent is sought on the invention entitled:

TITLE OF INVENTION
A PROCESS FOR THE RECOVERY OF LACTIC ACID BY CONTACTING AQUEOUS SOLUTIONS
CONTAINING THE SAME WITH A BASIC ORGANIC EXTRACTANT

SPECIFICATION IDENTIFICATION

The specification of which:

(complete (a), (b), or (c))

(a) ☐ is attached hereto.

NOTE: "The following combinations of information supplied in an oath or declaration filed on the application filing date with a specification are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirement of 37 C.F.R. § 1.63:

"(1) name of inventor(s), and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration on filing;

"(2) name of inventor(s), and attorney docket number which was on the specification as filed; or

"(3) name of inventor(s), and title which was on the specification as filed."

Notice of July 13, 1995 (1177 O.G. 60).

(b) ☒ was filed on 4/8/99, as ☒ Application No. 0 9 284,160 or ☐ and was amended on _____ (if applicable).

NOTE: Amendments filed after the original papers are deposited with the PTO that contain new matter are not accorded a filing date by being referred to in the declaration. Accordingly, the amendments involved are those filed with the application papers or, in the case of a supplemental declaration, are those amendments claiming matter not encompassed in the original statement of invention or claims. See 37 C.F.R. § 1.67.

NOTE: "The following combinations of information supplied in an oath or declaration filed after the filing date are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirement of 37 C.F.R. § 1.63:

"(1) name of inventor(s), and application number (consisting of the series code and the serial number; e.g., 08/123,456);

"(2) name of inventor(s), serial number and filing date;

"(3) name of inventor(s) and attorney docket number which was on the specification as filed.

"(4) name of inventor(s), title which was on the specification as filed and filing date;

"(5) name of inventor(s), title which was on the specification as filed and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration; or

"(6) name of inventor(s), title which was on the specification as filed and accompanied by a cover letter accurately identifying the application for which it was intended by either the application number (consisting of the series code and the serial number; e.g., 08/123,456), or serial number and filing date. Absent any statement(s) to the contrary, it will be presumed that the application filed in the PTO is the application which the inventor(s) executed by signing the oath or declaration."

Notice of July 13, 1995 (1177 O.G. 60), M.P.E.P. § 601(a), 6th ed., rev.3.

- (c) ☒ was described and claimed in PCT International Application No. US97/15844 filed on October 2, 1997 and as amended under PCT Article 19 on _____ (if any).

SUPPLEMENTAL DECLARATION (37 C.F.R. § 1.67(b))

(complete the following where a supplemental declaration is being submitted)

☐ I hereby declare that the subject matter of the

☐ attached amendment

☐ amendment filed on _____

was part of my/our invention and was invented before the filing date of the original application, above identified, for such invention.

ACKNOWLEDGMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information, which is material to patentability as defined in 37, Code of Federal Regulations, § 1.56,

(also check the following items, if desired)

☐ and which is material to the examination of this application, namely, information where there is a substantial likelihood that a reasonable Examiner would consider it important in deciding whether to allow the application to issue as a patent, and

☐ in compliance with this duty, there is attached an information disclosure statement, in accordance with 37 C.F.R. § 1.98.

PRIORITY CLAIM (35 U.S.C. § 119(a)-(d))

NOTE: "The claim to priority need be in no special form and may be made by the attorney or agent if the foreign application is referred to in the oath or declaration as required by § 1.63. The claim for priority and the certified copy of the foreign application specified in 35 U.S.C. § 119(b) must be filed in the case of an interference (§ 1.630), when necessary to overcome the date of a reference relied upon by the examiner, when specifically required by the examiner, and in all other situations, before the patent is granted. If the claim for priority or the certified copy of the foreign application is filed after the date the issue fee is paid, it must be accompanied by a petition requesting entry and by the fee set forth in § 1.17(i). If the certified copy is not in the English language, a translation need not be filed except in the case of interference; or when necessary to overcome the date of a reference relied upon by the examiner; or when specifically required by the examiner, in which event an English language translation must be filed together with a statement that the translation of the certified copy is accurate." 37 C.F.R. § 1.55(a).

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

(complete (d) or (e))

- (d) ☐ no such applications have been filed.
 (e) ☒ such applications have been filed as follows.

NOTE: Where item (c) is entered above and the International Application which designated the U.S. itself claimed priority check item (e), enter the details below and make the priority claim.

**PRIOR FOREIGN/PCT APPLICATION(S) FILED WITHIN 12 MONTHS
 (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION
 AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. § 119(a)-(d)**

COUNTRY (OR INDICATE IF PCT)	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR	PRIORITY CLAIMED UNDER 35 USC 119
Israel	119387	9 October 1996	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO

(Check the following item, if applicable)

- [] I hereby appoint the practitioner(s) associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.
- [] Attached, as part of this declaration and power of attorney, is the authorization of the above-named practitioner(s) to accept and follow instructions from my representative(s).

SEND CORRESPONDENCE TO

DIRECT TELEPHONE CALLS TO:
(Name and telephone number)

Ladas & Parry
26 West 61st Street
New York, N.Y. 10023

Peter D. Galloway
(212) 708-1905

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

09/04/100-102500

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name, as it should appear on the filing receipt and all other document.

NOTE: Each inventor must be identified by full name, including the family name, and at least one given name without abbreviation together with any other given name or initial, and by his/her residence, post office address and country of citizenship. 37 C.F.R. § 1.63(a)(3).

NOTE: Inventors may execute separate declarations/oaths provided each declaration/oath sets forth all the inventors. Section 1.63(a)(3) requires that a declaration/oath, inter alia, identify each inventor and prohibits the execution of separate declarations/oaths which each sets forth only the name of the executing inventor. 62 Fed. Reg. 53,131, 53,142, October 10, 1997.

Full name of sole or first inventor

1-00
Aharon _____ Meir _____ EYAL _____
(Given Name) (Middle Initial or Name) Family (Or Last Name)

Inventor's signature (x) A. d. Eyal

Date (x) July 1/1999 Country of Citizenship Israel

Residence Baitar Street 32, 93380 Jerusalem, Israel J L X

Post Office Address SAME AS ABOVE

Full name of second joint inventor, if any

2-00
Patrick _____ R. _____ GRUBER _____
(Given Name) (Middle Initial or Name) Family (Or Last Name)

Inventor's signature (x) Patrick R. Gruber

Date (x) 10/12/99 Country of Citizenship USA

Residence 10951 Flanders Court, N.E., Blaine, MN 55449 172

Post Office Address SAME AS ABOVE

3-00 Full name of third joint inventor, if any

Rod _____ R. _____ FISHER _____
(Given Name) (Middle Initial or Name) Family (Or Last Name)

Inventor's signature (x) Rod R. Fisher

Date (x) 13 Oct 99 Country of Citizenship USA

Residence 16820 South Shore Lane, Eden Prairie, MN 55346 MA

Post Office Address SAME AS ABOVE

*(check proper box(es) for any of the following added page(s)
that form a part of this declaration)*

- [x] Signature for fourth and subsequent joint inventors. *Number of pages added* 1

* * *

- [] Signature by administrator(trix), executor(trix) or legal representative for deceased or incapacitated inventor. *Number of pages added*

* * *

- [] Signature for inventor who refuses to sign or cannot be reached by person authorized under 37 C.F.R. § 1.47. Number of pages added

* * *

- [] Added page for signature by one joint inventor on behalf of deceased inventor(s) where legal representative cannot be appointed in time. (37 C.F.R. § 1.47)

- [] Added pages to combined declaration and power of attorney for divisional, continuation, or continuation-in-part (C-I-P) application.

[] Number of pages added _____

* * *

- ☐ Authorization of practitioner(s) to accept and follow instructions from representative.

*(If no further pages form a part of this Declaration,
then end this Declaration with this page and check the following item)*

[] This declaration ends with this page.

Practitioner's Docket No. U 012190-3

**ADDED PAGE TO COMBINED DECLARATION AND POWER OF
ATTORNEY FOR SIGNATURE BY FOURTH AND SUBSEQUENT INVENTORS**

Full name of fourth joint inventor, if any

Jeffrey

(Given Name)

(Middle Initial or Name)

KOLSTAD

Family (Or Last Name)

Inventor's signature (x)

Date (x) Oct 13, 1999 Country of Citizenship USA

Residence 16122 Ringer Road, Wayzata, MN 55391

Post Office Address SAME AS ABOVE

Full name of fifth joint inventor, if any

(Given Name)

(Middle Initial or Name)

Family (Or Last Name)

Inventor's signature

Date Country of Citizenship

Residence

Post Office Address

Full name of sixth joint inventor, if any

(Given Name)

(Middle Initial or Name)

Family (Or Last Name)

Inventor's signature

Date Country of Citizenship

Residence

Post Office Address